

論文の内容の要旨

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| 論文題目 | A Comparison of Surgical Models of Reflux Esophagitis in Mice |
| 和訳 | マウスを用いた逆流性食道炎モデルの比較 |
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Introduction: Research in esophageal adenocarcinoma has come to attention as a consequence of the increasing incidence of this type of tumor and its high morbimortality. Esophageal reflux is thought to be one of the causes of this type of cancer, and the surgical models used to study it generally use rats. We compared three types of reflux operation using mice, an important animal for genetic studies, to verify the suitability of this animal to study esophageal adenocarcinogenesis. In addition, we tested the expression of CDX2 and PDX1 in areas of intestinal metaplasia and adenocarcinoma. **Method:** C57Bl/6J mice aged 8 weeks were divided into the following groups: those undergoing esophagogastrorjejunostomy (EGJ), those undergoing esophageal separation and esophagojejunostomy (EJ), and those undergoing esophagojejunostomy with total gastrectomy (EJ/TG). The animals were euthanized 40 weeks after the operation, and the esophagus was analyzed regarding histological changes and immunohistochemical positivity of CDX2 and PDX1. **Results:** Intestinal metaplasia developed

in two operation groups (EGJ, 45.5%; EJ/TG, 15.4%; $p < .05$) and did not develop in the EJ group. Adenocarcinoma developed in 21.2% of the cases in the EGJ group, in 2.6% of the cases in the EJ/TG group, but did not develop in the EJ group. CDX2 was positive in all cases of metaplasia. PDX1 was positive in 80% of cases with metaplasia in the EGJ group and 50% of cases with metaplasia in the EJ/TG group. In total, PDX1 was positive in 71% of cases with metaplasia and 88% of cases with adenocarcinoma. **Discussion:** The operations resulted in rates of intestinal metaplasia formation in accordance with published rat studies; differences were observed, particularly in relation to the EJ model. EGJ had the highest rates of development of intestinal metaplasia and adenocarcinoma (which was not reported before with this model in mice). PDX1 expression in columnar metaplasia in human tissues was confirmed by our collaborators. PDX1 could be a marker of Barrett's esophagus in rodent GERD models and have a key role in columnar metaplasia development in the esophagus. **Conclusion:** EGJ was the most suitable esophageal reflux model in this species of mice. *Pdx1* may have a role in esophageal intestinal metaplasia development.